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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,516	02/07/2001	Wei-Yu Lo	12875-002001 / 0643-5299U	3185

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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/778,516	LO ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 February 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ they raise the issue of new matter (see Note below);
   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: *See Continuation Sheet*.
3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: *4 and 7-9*.

   Claim(s) rejected: *1-3,5,6 and 10-14*.

   Claim(s) withdrawn from consideration: _____.
8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

DAVID GUZO
PRIMARY EXAMINER

Continuation of 2. NOTE: The claims submitted with in the 20 February 2004 filing do not appear to contain any amendments. All of the claims are indicated as "Previously presented" or "Original" and there are no markings to indicate changes made..

Continuation of 5. does NOT place the application in condition for allowance because:

Claims 1-3, 5, 6 and 10-14 stand rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description for "a nucleic acid sequence encoding a protein which is involved in replication of the lactic acid bacteria plasmid".

The Examiner contends that the specification provides no limitation on how the protein of the claims is "involved in" replication of the lactic acid bacterial plasmid and therefore broadly encompasses any protein that might reasonably be considered to promote replication of the plasmid. In response, Applicant points to the examples, which teach a single protein involved in replication of a lactic acid bacterial plasmid (i.e., RepA). Applicant urges that because RepA protein binds to DNA and is directly involved in bacterial plasmid replication, one skilled in the art would clearly recognize that the claimed vector has a nucleic acid sequence encoding a DNA-binding protein involved in plasmid replication. Applicant contends, "[g]iven the knowledge possessed by those skilled in the art, the specification conveys that Applicants were in possession of use of RepA and its equivalents to practice the claimed invention at the time the invention was filed" (page 6).

These arguments have been fully considered but are not deemed persuasive because the rejected claims are not limited to a vector comprising RepA or its equivalents. Applicant seems to be arguing that, because the RepA protein provided as an example of a protein involved in replication of a lactic acid bacterial plasmid is a DNA-binding protein, the protein of the claims is limited to being a DNA-binding protein. Applicant is reminded, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims (MPEP 2145(V)). The claims do not recite that the protein involved in replication of the lactic acid bacterial plasmid must be RepA or its equivalent and there is nothing in the specification to indicate that the protein is so limited.

Next, Applicant argues that DNA-binding proteins involved in DNA replication are highly conserved among different species throughout evolution and a replication protein of one species often functions well in another species. Applicant urges, "a lactic acid bacterial replication protein can be replaced by its counterpart in a different species or its non-conserved mutants, including man-made variants" (page 6). Applicant also provides two exhibits (i.e., Kelly et al. and Brill et al.), which show that the DNA binding domain of single-stranded DNA-binding proteins is conserved. This argument and the Exhibits are not deemed persuasive. The issue at hand is not whether homologues of DNA-binding proteins involved in DNA replication would function across species because the claims are not limited to DNA-binding proteins (Id.). Again, Applicant is arguing limitations that are neither explicitly nor implicitly present.

Applicant's arguments have been fully considered but are not deemed persuasive either individually or as a whole. Therefore the claims stand rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description.

Claim 13 is rejected as lacking enablement for a DNA vaccine composition comprising the broad scope of "an antigenic gene".

In response to the rejection and arguments of record, Applicant disagrees with the Examiner's contention that, given the number of inoperative combinations within the scope of the claimed invention, the skilled artisan would be forced to experiment unduly in order to practice the claimed invention. Applicant alleges that inoperative or operative vaccines can be determined with expenditure of no more effort than is normally required in the art, but provides nothing to substantiate this assertion. The Examiner's position is based on the tremendous scope of the claim, which encompasses a DNA vaccine comprising any antigenic gene, and the unpredictability of obtaining a protective immune response with any given antigenic gene (see especially pages 8 and 9 of the First Office Action on the Merits, mailed 27 November 2001), which require that the skilled artisan seeking to use the claimed invention engage in blind trial and error experimentation to make and test each embodiment of the invention.

Applicant contends that it is not necessary to test each vaccine of claim 13 to show that it is operative. Applicant alleges that In re Angstadt, 190 USPQ 214,218 (CCPA 1976) supports the position that applicants are not required to disclose every species encompassed by their claims even in an unpredictable art. This argument is not deemed persuasive because it has never been the Examiner's contention that Applicant is required to disclose every species within the scope of the claimed genus. The statement from the Office Action cited by applicant is directed to the amount of experimentation required to practice the full scope of the claims, it is not a statement of Applicant's burden. If the invention is disclosed in such a way as to enable the skilled artisan to make and use the full scope of the claimed subject matter without engaging in undue experimentation, it is not necessary to disclose each and every embodiment encompassed by the claims. However, that is not the case here. In Angstadt the Court states, "[h]aving decided that appellants are not required to disclose every species encompassed by their claims even in an unpredictable art such as the present record presents, each case must be determined on its own facts" (page 218; emphasis added). Thus, the court clearly indicates that adequacy of the disclosure with regards to enablement must be determined based on the facts of the individual case.

The facts that lead to the decision in Angstadt are clearly different from those of the instant case. In Angstadt, the appellants' invention was the use of a complex catalyst comprising a hexaalkylphosphoramide and a transition metal salt to catalyze the oxidation of secondary or tertiary alkylaromatic hydrocarbons to form hydroperoxides. Appellants had provided the skilled artisan with a large but finite list of transition metal salts from which to choose in preparing such a complex catalyst. Appellants had actually carried out 40 runs using various transition metal salts and hexaalkylphosphoramides. If one skilled in this art wished to make and use a transition metal salt other than those disclosed in appellants' 40 runs, he would merely read appellants' specification for directions how to make and use the catalyst complex to oxidize the alkylaromatic hydrocarbons, and could then determine whether hydroperoxides are, in fact, formed. The process discovered by the appellants was not complicated, and there was no indication that special equipment or unusual reaction conditions must be provided when practicing the invention. One skilled in this art would merely have to substitute the correct mass of a transition metal salt for the transition metal salts disclosed in appellants' 40 runs. Thus, the court had no basis for concluding that persons skilled in this art, armed with the specification and its 40 working examples, would not easily be able to determine which catalyst complexes within the scope of the claims work to produce hydroperoxides and which do not.

In contrast, in the instant case, the antigenic gene of the claim is unlimited, the processes involved in eliciting an effective immune response using a DNA vaccine are extremely complex and the specification does not provide a single working example of the claimed invention. Clearly the courts decision based on the facts of Angstadt do not indicate that the instant claims are enabled. In contrast, the facts of the instant case have been fully considered according to the guidelines set forth in In re Wands (see especially the 27 November 2001 Office Action) and based on that analysis the instant claim 13 has been found to lack enablement.

Applicant's arguments have been fully considered but are not deemed persuasive either individually or as a whole; therefore, claim 13 stands rejected under 35 U.S.C. §112, first paragraph, a lacking an enabling disclosure..